Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Performing the embryo transfer: a guideline.

Bibliographic Source(s)

Practice Committee of the American Society for Reproductive Medicine. Performing the embryo transfer: a guideline. Fertil Steril. 2017 Apr;107(4):882-96. [149 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
NO	Disclosure of Guideline Funding Source
	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
UNKNOWN	Multidisciplinary Group
UNKNOWN	Methodologist Involvement
	Patient and Public Perspectives

	Use of a Systematic Review of Evidence
▮▮▮▮▯	Search Strategy
▮▮▮▮▯	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▯▯	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▯▯	Rating the Strength of Recommendations
▮▮▮▯▯	Specific and Unambiguous Articulation of Recommendations
▮▯▯▯▯	External Review
▮▮▮▯▯	Updating

Recommendations

Major Recommendations

Definitions for the level of evidence (Level I-III) and strength of the recommendations (Grade A-C) are given at the end of the "Major Recommendations" field.

Is Patient Preparation, including Acupuncture, Relaxant, Sedation, or Antibiotics, Before Embryo Transfer Necessary and Does It Affect Pregnancy and Live-birth Rates?

Acupuncture

Summary Statement

There is fair evidence that acupuncture performed around the time of embryo transfer does not improve live-birth rates in in vitro fertilization (IVF). (Grade B)

Analgesics

Summary Statement

There is insufficient evidence to recommend for or against analgesics to improve IVF-embryo transfer outcomes. (Grade C)

Anesthesia

Summary Statement

There is insufficient evidence that anesthesia during embryo transfer improves pregnancy rates. Given that there is no clear benefit and that there are inherent risks associated with anesthesia, routine

anesthesia is not recommended to improve IVF-embryo transfer outcomes. (Grade C)

Massage

Summary Statement

There is insufficient evidence to recommend for or against massage therapy to improve IVF-embryo transfer outcomes. (Grade C)

Transcutaneous Electrical Acupoint Stimulation

Summary Statement

There is fair evidence based on only one randomized controlled trial (RCT) that transcutaneous electrical acupoint stimulation (TEAS) improves IVF-embryo transfer (ET) outcomes (Grade B). However, given the lack of any other studies, a recommendation for or against TEAS to improve IVF-ET outcomes cannot be made.

Whole-Systems Traditional Chinese Medicine (WS-TCM)

Summary Statement

There is insufficient evidence to recommend for or against WS-TCM to improve IVF-embryo transfer outcomes. (Grade C)

Prophylactic Antibiotics

Summary Statement

There is fair evidence based on a single RCT that an antibiotic regimen that includes amoxicillin and clavulanic acid given on the day before and the day of embryo transfer does not improve pregnancy rates (Grade B). Given these results and the lack of other evidence in the literature to support prophylactic antibiotics at embryo transfer, a recommendation for routine prophylactic antibiotics cannot be made.

Does Physician Preparation, Including the Use of Sterile Latex-free Gloves, Before an Embryo Transfer Procedure Affect Pregnancy and Live-birth Rates?

Summary Statement

There is fair evidence based on one, single-center RCT that powdered gloves worn during embryo transfer do not have an adverse effect on pregnancy rates. (Grade B). No specific type of glove is recommended for embryo transfer.

Does Routine Use of Abdominal Ultrasound for Guidance During Embryo Transfer Improve Pregnancy and Live-birth Rates?

Summary Statements

- There is good evidence based on 10 RCTs to recommend TA ultrasound guidance during embryo transfer to improve clinical pregnancy rate and live-birth rate. (Grade A)
- While selected ultrasound guidance for an anticipated difficult embryo transfer may be an alternative to routine ultrasound guidance, there is insufficient evidence to recommend for or against this practice. (Grade C)

Does Removing Mucus from the Endocervical Canal Improve Pregnancy and Live-birth Rates?

Summary Statement

There is fair evidence based on one RCT and one prospective cohort study that there is a benefit to removing cervical mucus at the time of embryo transfer to improve clinical pregnancy and live-birth rates. (Grade B)

Does the Type of Catheter Used for Embryo Transfer Affect Pregnancy and Live-birth Rates?

Summary Statement

There is good evidence to recommend the use of a soft embryo transfer catheter to improve IVF-embryo transfer pregnancy rates. (Grade A). Data on live-birth rates and specific types of soft catheters are limited.

Does Positioning the Catheter at the Time of Embryo Transfer Affect IVF-Embryo Transfer Implantation, Pregnancy, and Live-birth Rates?

Summary Statements

There is fair evidence based on six studies (two RCTs and four cohort studies) that embryo transfer catheter placement affects implantation and pregnancy rates. (Grade B)
There is fair evidence based on seven studies (three RCTs and four cohort studies) that placement of the catheter tip in the upper or middle (central) area of the uterine cavity, greater than 1 cm from the fundus for embryo expulsion, optimizes pregnancy rates. (Grade B)
There is insufficient evidence for more specific recommendations regarding the positioning of the catheter at the time of embryo transfer. (Grade C)

Does the Time Interval before Withdrawing the Catheter Affect IVF-Embryo Transfer Pregnancy and Live-birth Rates?

Summary Statement

There is fair evidence based on one RCT and one cohort study to recommend immediate withdrawal of the embryo transfer catheter after embryo expulsion. (Grade B)

Is the Presence of Mucus on the Catheter (After It Is Removed) Associated with Pregnancy and Live-birth Rates?

Summary Statement

There is fair evidence based on seven cohort studies that the presence of mucus on the embryo transfer catheter, once it is withdrawn, is not associated with a lower clinical pregnancy rate or live-birth rate. (Grade B)

Does the Presence of Blood on the Catheter (Once It Is Withdrawn) Make a Difference in Pregnancy or Live-birth Rate?

Summary Statement

Given the mixed results of studies, there is insufficient evidence to state conclusively that the presence of blood on the catheter, once it is withdrawn, is associated with implantation or pregnancy rates. (Grade C)

Does the Rate of Injection of the Catheter Load Affect Pregnancy and Live-birth Rates?

Summary Statement

Given the paucity of data, there is insufficient evidence to recommend any specific injection speed of the catheter at the time of embryo transfer. (Grade C)

Do Retained Embryos in the Transfer Catheter and Immediate Re-transfer of Them Affect Implantation, Clinical Pregnancy, or Spontaneous Abortion Rates?

Summary Statement

There is fair evidence based on the secondary outcome of one RCT, nine cohort studies, and one series that retained embryos in the transfer catheter and immediate re-transfer do not affect implantation, clinical pregnancy, or spontaneous abortion rates. (Grade B)

Does Bed Rest or Ambulation Affect IVF-Embryo Transfer Pregnancy and Live-birth Rates?

Summary Statement

There is good evidence not to recommend bed rest after embryo transfer. (Grade A)

Recommendations

Embryo transfer is considered a critical step in the IVF process. Extensive literature exists regarding all aspects of embryo transfer, which supports its importance to overall IVF success. While there are insufficient data to provide guidance on a number of techniques used during embryo transfer, the literature does provide guidance for many aspects of this critical component of IVF.

The following interventions are supported by the literature for improving pregnancy rates:

Abdominal ultrasound guidance for embryo transfer
Removal of cervical mucus
Use of soft embryo transfer catheters
Placement of embryo transfer tip in the upper or middle (central) area of the uterine cavity, greater than 1 cm from the fundus, for embryo expulsion
Immediate ambulation once the embryo transfer procedure is completed

The following interventions have been shown not to be beneficial for improving pregnancy rates:

Acupuncture
Analgesics, massage, general anesthesia, whole systems – traditional Chinese medicine
Prophylactic antibiotics to improve embryo transfer outcomes
Waiting after expulsion of embryos for any specific period of time before withdrawing the embryo transfer catheter

Definitions

Level of Evidence

Level I: Evidence obtained from at least one properly designed randomized, controlled trial.

Level II-1: Evidence obtained from well-designed controlled trials without randomization.

Level II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

Level II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

Level III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

Systematic reviews/meta-analyses were individually considered and included if they followed a strict methodological process and assessed relevant evidence.

Strength of Recommendations

Grade A: There is good evidence to support the recommendations, either for or against.

Grade B: There is fair evidence to support the recommendations, either for or against.

Grade C: There is insufficient evidence to support the recommendations, either for or against.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Infertility

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Internal Medicine

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To examine the various steps of the Common Practice Protocol by a systematic review of the literature to determine which of the steps, if any, are supported by sufficient data for performing embryo transfer

Target Population

Women undergoing in vitro fertilization (IVF)

Interventions and Practices Considered

1. Transabdominal (TA) ultrasound guidance
2. Removal of cervical mucus
3. Use of soft embryo transfer catheters
4. Immediate withdrawal after embryo expulsion
5. Placement of embryo transfer tip in the upper or middle (central) area of the uterine cavity, greater than 1 cm from the fundus, for embryo expulsion
6. Immediate ambulation once embryo transfer procedure is completed

Note:

- The following interventions were considered, but a recommendation cannot be made: analgesics, massage therapy, transcutaneous

electrical acupoint stimulation (TEAS), whole systems–traditional Chinese medicine, selected ultrasound guidance for anticipated difficult transfers, prophylactic antibiotics (including amoxicillin and clavulanic acid), injection speed of catheter
- The following interventions were considered but not recommended: acupuncture, routine anesthesia

Major Outcomes Considered

- Pregnancy rate
- Live-birth rate
- Implantation rate

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

This clinical practice guideline was based on a systematic review of the literature. A systematic literature search of relevant articles was performed in the electronic database MEDLINE through PubMed in December 2016, with a filter for human subject research. No limit or filter was used for time period or English language, but articles were subsequently culled for English language. A combination of the following medical subject headings or text words/keywords were used: acupuncture; acupuncture therapy; afterloading; ambulation; analgesia; analgesic; analgesics; anesthesia; anti anxiety; antibacterial hand soaps; antibiotic; antibiotics; antibiotic prophylaxis; bed rest; bedrest; birth; bleeding; blastocyst transfer; blood; catheter; catheter remains; catheter remnants; catheterization; catheterization/adverse effects; catheterization/ methods; cervix; Chinese medicine; cleanse; cleanser; cleansing; deposition; disinfection; duration; ejection; embryo retention; embryo transfer; embryo transfer catheter; embryo transfer/instrumentation; embryo transfer/methods; embryo transfer protocol; embryo transfer techniques; endometrial; endometrial cavity; endometrium; expel; expulsion; flushing; gloves; hand disinfection; hand hygiene; hand washing; hand washing/ behavior; hand washing/behaviors; hand disinfectant; hand disinfectants; hand washing/glove; implantation; injection; in vitro fertilization; IVF; load; loading; massage; medicine, Chinese traditional relaxant; mucus; mucous; physician; physician's role; placement; plunge; plunger; pregnancy; pressure; recumbency; recumbent; recumbent position; recumbent posture; release; replacement; rest; retained embryos; sedation; simulation; skin scrub; speed; stiletto; stylet; stylette; success; success rate; supine; surgical gloves; surgical scrub; time; time factors; time interval; transcutaneous electrical acupoint stimulation; transcutaneous electrical nerve stimulation; transfer techniques; ultrasound; ultrasound guidance; ultrasound guided embryo transfer; uteri; uterus; vaginal flush; vaginal preparation.

Initially, titles and abstracts of potentially relevant articles were screened and reviewed for inclusion/exclusion criteria. Protocols and results of the studies were examined according to specific inclusion criteria. Only studies that met the inclusion criteria were assessed in the final analysis. Studies were eligible if they met one of the following criteria: level I or II studies that assessed the effectiveness of a procedure correlated with an outcome measure (pregnancy, implantation, or live-birth rates); meta-analyses; and relevant articles from bibliographies of identified articles. This guideline focuses principally on pregnancy rate since most of the studies report pregnancy rates rather than live-birth rates.

Three members of an independent task force reviewed the full articles of all citations that possibly matched the predefined selection criteria. Final inclusion or exclusion decisions were made on

examination of the articles in full. Disagreements about inclusion among reviewers were discussed and solved by consensus or arbitration after consultation with an independent reviewer/epidemiologist.

Tables listing inclusion/exclusion criteria are available online as Supplemental Material (see the "Availability of Companion Documents" field.)

Number of Source Documents

Number of studies identified in electronic search and from examination of reference lists from primary and review articles: 2,086. Number of studies included: 143.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Level of Evidence

Level I: Evidence obtained from at least one properly designed randomized, controlled trial.

Level II-1: Evidence obtained from well-designed controlled trials without randomization.

Level II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

Level II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled trials might also be regarded as this type of evidence.

Level III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.

Systematic reviews/meta-analyses were individually considered and included if they followed a strict methodological process and assessed relevant evidence.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The quality of the evidence was evaluated using the grading system found in the "Rating Scheme for the Strength of the Evidence" field and is assigned for each reference in the bibliography (see the original guideline document).

Systematic reviews/meta-analyses were individually considered and included if they followed a strict methodological process and assessed relevant evidence.

When current meta-analyses were not available to combine existing data, selected meta-analyses of studies were performed by the American Society for Reproductive Medicine (ASRM) Practice Committee to estimate the pooled relative risk (RR) ratios of outcomes of interest. Statistical analyses and construction

of forest and funnel plots were performed with Stata version 12.1. RR ratios, and 95% confidence intervals (CIs) were calculated for each outcome. Random effects models were used for the meta-analyses. Heterogeneity was assessed with the use of the I^2 test. Publication bias was assessed by constructing funnel plots.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

A systematic review of the literature was conducted which examined each of the major steps of embryo transfer. Recommendations made for improving pregnancy rates are based on interventions demonstrated to be either beneficial or not beneficial.

The literature was reviewed to answer the following questions:

- Is patient preparation, including acupuncture, relaxant, sedation, or antibiotics, before embryo transfer necessary and does it affect pregnancy and live-birth rates?
- Does physician preparation, including the use of sterile latex-free gloves, before an embryo transfer procedure affect pregnancy and live-birth rates?
- Does routine use of abdominal ultrasound for guidance during embryo transfer improve pregnancy and live-birth rates?
- Does removing mucus from the endocervical canal improve pregnancy and live-birth rates?
- Does the type of catheter used for embryo transfer affect pregnancy and live-birth rates?
- Does positioning the catheter at the time of embryo transfer affect IVF-embryo transfer implantation, pregnancy, and live-birth rates?
- Does the time interval before withdrawing the catheter affect IVF-embryo transfer pregnancy and live-birth rates?
- Is the presence of mucus on the catheter (after it is removed) associated with pregnancy and live-birth rates?
- Does the presence of blood on the catheter (once it is withdrawn) make a difference in pregnancy or live-birth rate?
- Does the rate of injection of the catheter load affect pregnancy and live-birth rates?
- Do retained embryos in the transfer catheter and immediate re-transfer of them affect implantation, clinical pregnancy, or spontaneous abortion rates?
- Does bed rest or ambulation affect IVF-embryo transfer pregnancy and live-birth rates?

The strength of the recommendations was evaluated using the grading system found in the "Rating Scheme for the Strength of the Recommendations" field.

In designing the American Society for Reproductive Medicine (ASRM) embryo transfer protocol, data from the survey of medical directors helped determine the most commonly used technique when the literature did not inform an outcome-based recommendation.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Grade A: There is good evidence to support the recommendations, either for or against.

Grade B: There is fair evidence to support the recommendations, either for or against.

Grade C: There is insufficient evidence to support the recommendations, either for or against.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This document was reviewed by American Society for Reproductive Medicine members and their input was considered in the preparation of the final document.

The Practice Committee and the Board of Directors of the American Society for Reproductive Medicine have approved this report.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each summary statement that supports the recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- With regard to the transfer of fresh embryos in eight randomized controlled trials (RCTs) and four cohort studies, transabdominal (TA) ultrasound—guided embryo transfer was found to improve the implantation rate and/or pregnancy rate, clinical or ongoing clinical pregnancy rates, and/or live-birth rate. Studies have also shown improved outcomes using ultrasound guidance with frozen embryo transfer and programmed recipient cycles using donor eggs.
- One RCT showed improved clinical pregnancy rate and live-birth rate with the removal of cervical mucus. The clinical pregnancy rate was significantly higher in the group that had mucus aspiration compared with the group with no aspiration in the cohort study.
- The majority of the studies found that embryo placement impacted pregnancy rates, with pregnancy rates highest when the embryo was placed in the upper or middle area of the uterine cavity, at least 1 cm away from the fundus.
- The placement of the outer catheter may also affect pregnancy rates. In a cohort study of 408 patients who underwent embryo transfer, overall pregnancy rates were significantly better in those patients for whom the outer sheath did not go beyond the internal os compared with patients for whom the catheter was placed through the internal os.
- One study demonstrated that the live-birth rates were significantly higher in the no bed rest group when compared to 10 minutes of rest.

Refer to the "Clinical Practice" section in the original guideline document for details about potential benefits of specific interventions.

Potential Harms

It has been suggested that removing cervical mucus might stimulate uterine contractility or cervical bleeding, with a possible negative impact on pregnancy outcomes.

Refer to the "Clinical Practice" section in the original guideline document for details about potential harms of specific interventions.

Qualifying Statements

Qualifying Statements

This report was developed under the direction of the Practice Committee of the American Society for Reproductive Medicine as a service to its members and other practicing clinicians. Although this document reflects appropriate management of a problem encountered in the practice of reproductive medicine, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Other plans of management may be appropriate, taking into account the needs of the individual patient, available resources, and institutional or clinical practice limitations.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Practice Committee of the American Society for Reproductive Medicine. Performing the embryo transfer: a guideline. Fertil Steril. 2017 Apr;107(4):882-96. [149 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Apr

Guideline Developer(s)

American Society for Reproductive Medicine - Nonprofit Organization

Source(s) of Funding

American Society for Reproductive Medicine (ASRM)

Guideline Committee

Practice Committee of the American Society for Reproductive Medicine (ASRM)

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Financial Disclosures/Conflicts of Interest

All Committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the Committee who were found to have conflicts of interest based on the relationships disclosed did not participate in the discussion or development of this document.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American Society for Reproductive Medicine (ASRM) Web site .

Availability of Companion Documents

The following is available:

> Practice Committee of the American Society for Reproductive Medicine, et al. ASRM standard embryo transfer protocol template: a committee opinion. Fertil Steril. 2017 Apr;107(4):897-900. Available for purchase from the Fertility and Sterility Journal Web site .

A continuing medical education (CME) activity on embryo transfer is also available from the American Society for Reproductive Medicine (ASRM) Web site .

The supplemental material is available to subscribers from the Fertility and Sterility Journal Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on November 29, 2017. The information was verified by the guideline developer on December 21, 2017.

This NEATS assessment was completed by ECRI Institute on October 16, 2017. The information was verified by the guideline developer on December 21, 2017.

Copyright Statement

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